

ACTIVATION OF PHAGOCYTES FROM PERIPHERAL HUMAN BLOOD BY *Paracoccidioides brasiliensis* AND ENTEROPATHOGENIC *Escherichia coli*. PRODUCTION OF SUPEROXIDE ANION AND MODULATION BY MELATONIN HORMONE

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ABSTRACT: The production of free radicals by phagocytes plays a key role in the host defense against invasive microorganisms. Extensive epidemiological evidences have shown that various bacterial and fungal infections are associated with hormones, age, and sex. In the present investigation, we verified the role of melatonin in the activation of blood phagocytes in the presence of *P. brasiliensis* and enteropathogenic *E. coli* (EPEC), in relation to sex. Blood samples were collected from 25 male volunteers and 21 female volunteers, and the cells were separated into two populations: mononuclear (MN) and polimorfonuclear (PMN). We observed that MN and PMN phagocytes release superoxide anion. The superoxide release was increased when the cells were stimulated by Phorbol Myristate Acetate (PMA). The phagocytes from females showed more sensitivity when stimulated by PMA. When the cells were incubated with EPEC or *P. brasiliensis*, we observed that phagocytes from females and males showed similar superoxide release, and no difference was observed between fungal and bacterial stimuli. The phagocytes from females, incubated with EPEC or *P. brasiliensis*, showed an increased superoxide release in comparison with the phagocytes from males. Melatonin hormone showed immunomodulation action on the superoxide release by phagocytes, and this action was sex-dependent. The phagocytes from females, stimulated by melatonin, independent on the cell type, showed significantly increased superoxide release. The phagocytes from males presented differences between the cell types. The levels of

superoxide release were higher in PMN phagocytes than in MN. When the MN phagocytes were stimulated by melatonin and incubated with *P. brasiliensis* or EPEC, equivalent levels of superoxide release were observed in comparison with those cells incubated only with EPEC or *P. brasiliensis*. When the PMN phagocytes were stimulated by melatonin and incubated with *P. brasiliensis* or EPEC, they showed significant increase in the superoxide release in comparison with those cells incubated only with EPEC or *P. brasiliensis*. The PMN phagocytes from females showed more superoxide release in comparison with PMN phagocytes from males. Our results indicate that melatonin acts as an immunomodulator agent and may represent an additional mechanism of protection against bacterial and fungal infections.

KEY WORDS: *P. brasiliensis*, *E. coli*, phagocytes, melatonin.

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